

Effects of Vitamin E and/or Selenium Deficiency on the Cooxidation of Benzo(a)pyrene-7,8-dihydrodiol mediated by Prostaglandin Synthetase catalyzed Arachidonic Acid Metabolism. C. Channa Reddy, C. E. Thomas, E. J. Massaro and R. W. Scholz. The Pennsylvania State University, University Park, PA 16802 USA.

Most recent investigations have revealed that an important and intriguing aspect of prostaglandin biosynthesis is the generation of extremely reactive electrophiles including free radicals via cyclooxygenase catalyzed arachidonic acid (A.A.) metabolism. It has been demonstrated that these oxygen radicals are involved in the cooxidation of various xenobiotics including polycyclic aromatic hydrocarbons. Also, it has been suggested in the literature that antioxidants can prevent the cooxidation of xenobiotics mediated by cyclooxygenase pathway. To investigate this phenomenon further, we have studied the effects of dietary alterations of vitamin E (E) and Selenium (Se), two of the major antioxidant defense mechanism(s) of the body, on the cooxidation of benzo(a)pyrene-7,8-dihydrodiol (BP-diol) via the cyclooxygenase catalyzed A.A-dependent system and compared with the NADPH-dependent cytochrome P-450 mixed function oxidase catalyzed system. The experiments were conducted with lung microsomes obtained from Long-Evans Hooded male rats fed on chemically-defined purified diets with documented deficiencies of E, Se or both. As measured by the formation of BP tetrols, E deficiency resulted in an approximate increase of 2-3 fold in the oxidation of BP-diol mediated by the A.A-dependent system. However, the NADPH-dependent BP-diol oxidation was not affected by E deficiency. Similarly, E deficiency had resulted in an increased binding of BP diol metabolites to DNA and protein in the A.A-dependent system and had no appreciable effect on the NADPH-dependent system. In contrast, Se deficiency caused significant increase in the formation of BP-tetrols and covalent binding of BP-diol metabolites to DNA and protein in the NADPH-dependent system but showed only marginal effects on the A.A-dependent system. The effects of the addition of purified glutathione S-transferases having glutathione peroxidase activity and Se-dependent glutathione peroxidase on the oxidation and covalent binding of BP-diol and its metabolites will be presented.